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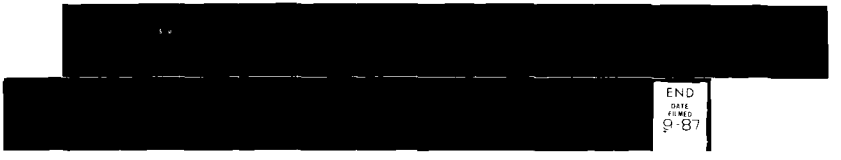

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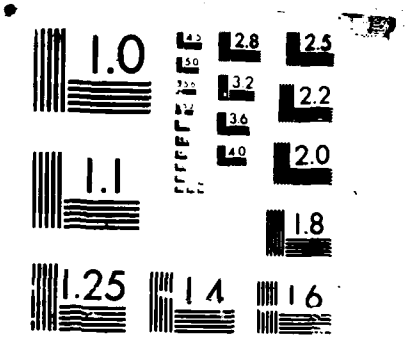

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TREATMENT OF LASER INDUCED RETINAL INJURIES

ANNUAL REPORT

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The effect of argon laser irradiation of the retina at various energy levels on PGE_2 production by the retina-choroid, and PGE_2 and protein accumulation in the vitreous cavity, was investigated and compared to the effects of sham exposures. The effect of steroid treatment on PGE_2 levels following laser exposure was also examined. Results showed that both single and multiple suprathreshold applications were characterized by a biphasic increase in retinal PGE_2 production, whereas multiple subthreshold exposure elicited an increase in PGE_2 production of much longer duration. In eyes subjected to

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sham exposure, the increase in retinal PGE_2 production was evident as a single peak. Moreover laser-induced retinal burns at most of the energy levels studied, as well as sham exposure resulted in an accumulation of PGE_2 and/or protein in the vitreous body.

The increases in PGE_2 and protein within the vitreous, when present, did not always conincide, and were noted at different time intervals following the various exposures studied. After multiple laser applications at either supra- or subthreshold energy levels, as well as after sham exposure of short duration, a correspondence was seen between the increase in vitreal PGE_2 levels and the increase in PGE_2 production by the retina-choroid. Following suprathreshold exposures, both single and multiple, the biphasic increase in vitreal protein levels and the biphasic increase in retinal PGE_2 production also coincided. However, multiple subthreshold expsoures did not elicit an increase in vitreal PGE_2 levels, despite the prolonged increase in retinal PGE_2 production observed in these eyes. Vitreal protein levels were increased for a short period after sham exposure of short duration.

Steroid treatment following a single laser application prevented the increase in retinal PGE_2 production as well as the augmentation of vitreal PGE_2 and protein levels.

Thus, the increase in PGE_2 production by the retina of eyes subjected to laser irradiation is related to the energy levels used. The accumulation of PGE_2 and protein in the vitreous after laser exposure is related to both the energy levels used and the integrity of the blood-retina barrier.

SUMMARY

The effect of argon laser irradiation of the retina at various energy levels on PGE_2 production by the retina-choroid and PGE_2 and protein accumulation in the vitreous cavity was investigated and compared to the effects of sham exposures. The effect of steroid treatment on PGE_2 levels following laser exposure was also examined. Results showed that both single and multiple suprathreshold applications were characterized by a biphasic increase in retinal PGE_2 production, whereas multiple subthreshold exposure elicited an increase in PGE_2 production of much longer duration. In eyes subjected to sham exposure, the increase in retinal PGE_2 production was evident as a single peak. Moreover, laser-induced retinal burns at most of the energy levels studied, as well as sham exposure, resulted in an accumulation of PGE_2 and/or protein in the vitreous body.

The increases in PGE_2 and protein within the vitreous, when present, did not always coincide, and were noted at different time intervals following the various exposures studied. After multiple laser applications at either supra- or subthreshold energy levels, as well as after sham exposure of short duration, a correspondence was seen between the increase in vitreal PGE_2 levels and the increase in PGE_2 levels and the increase in PGE_2 production by the retina-choroid. Following supra-threshold exposures, both single and multiple, the biphasic increase in vitreal protein levels and the biphasic increase in retinal PGE_2 production coincided. However, multiple subthreshold exposures did not elicit an increase in vitreal PGE_2 levels, despite the prolonged increase in retinal PGE_2 production observed in these eyes. Vitreal protein levels were increased for a short period after sham exposure of short duration.

Steroid treatment following a single laser application prevented the increase in retinal PGE_2 production as well as the augmentation in vitreal PGE_2 and protein levels.

Thus, the increase in PGE_2 production by the retina of eyes subjected to laser irradiation is related to the energy levels used. The accumulation of PGE_2 and protein in the vitreous after laser exposure and is related to both the energy levels used and the integrity of the blood-retina barrier.

FORWORD

In conducting the reserch described in this report, the investigation adhered to the "Guide for the Care and Use of Laboratory Animals" prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council (DHEW Publication No. (NIH) 78-23 Revised 1978).

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Introduction

Laser instruments are used in the battlefield, as well as in medicine, industry and communication, and it is certain that future armed conflict will result in many laser-induced eye injuries. Such injuries may cause temporary or permanent visual incapacitation. Their severity depends on the extent of the burn to the retina, the part of the eye most vulnerable to laser irradiation. The area surrounding the retinal laser site, which is a few times larger in diameter than the laser lesion itself, is also subject to inflammatory reaction and subsequent scarring. Any measure that will reduce this inflammation will accelerate healing, diminish the extent of scarring, and improve the visual prognosis of the patient.

Our investigation on the ocular reaction to laser irradiation was based on two hypothesis: (1) prostanoids are involved in laser-induced retinal burns; and (2) anti-inflammatory drugs that inhibit arachidonic acid metabolism - and thus decrease prostanoid production - will reduce retinal inflammation and accelerate healing.

The results of our studies during the first year of our investigation confirmed our hypothesis concerning the involvement of prostanoids in suprathreshold laser-induced retinal burns. We demonstrated that following multiple argon laser applications to the retina: (1) production of prostaglandins of type E_2 (PGE_2) by the retina-choroid is augmented in a biphasic fashion; (2) this PGE_2 accumulates in the vitreous, it reaches levels corresponding to those in the traumatized retina; and (3) protein levels in the vitreous persistently increase over one week follow-up.

During the second year we have been dealing with three subjects:
(1) prostanoid involvement following sham exposure for long or short duration; (2) prostanoid involvement following a single argon laser-induced retinal lesion and steroid treatment; (3) prostanoid involvement in subthreshold laser-induced retinal burns.

Methodology

Pigmented Dutch rabbits of either sex weighing 1.5 to 2.0 kg were used. All animals were anesthetized with 35/mg ketamine and 5 mg/kg xylazine.

Sham Exposure. Sham exposure involved pupil dilatation, contact lens fitting and illumination by the slit lamp attached to the argon laser (the identical prelasing procedure undergone by the experimental groups), but without irradiation.

Animals subjected to sham exposure were divided into two groups according to the duration of the illumination:

(1) long sham exposure -- illumination through the contact lens by the slit lamp was continued for a period sufficient to produce 30 laser burns;

(2) short sham exposure -- illumination throught the contact lens was continued for a period sufficient to produce a single laser burn.

Argon laser exposure. A continuous wave argon laser was used (Lasertek, 265 Excitor). The laser beam was focused on the retina through a Goldmann coated lens. Laser application involved either a single suprathreshold burn at power setting of 200 milliwatt, spot size 500 and duration 0.5 seconds, subthreshold burns consisted of 30 applications set as far apart as possible at the posterior pole outside the macula or optic nerve head at power setting of 20 milliwatt, spot size 60-70 u and duration 0.2 seconds, and were not visible ophthalmoscopically.

Following sham or laser exposure, animals were sacrificed using an overdose of pentobarbitone at various time intervals. The eyes were enucleated and the retina-choroid was dissected separately from the vitreous and sclera. One group of animals subjected to a single laser application was given steroid treatment (as described below); these were also sacrificed at the various time intervals.

Sample preparation. The retina-choroid preparation from each eye was placed in a vial containing 0.6 ml Krebs Ringer Bicarbonate Heppes buffer, pH 7.4, in a slow shaking bath at 37°C for 15 minutes. At the end of the incubation period, the tissues were removed, and samples were taken from the incubation media for PGE_2 determination.

The vitreous body from each animal was placed separately in another vial with the same buffer in a slow shaking bath at 37°C for 15 minutes. Samples for

PGE_2 determination. PGE_2 levels were determined using a radioimmunoassay with a specific antibody on PGE_2, as performed during the 1984 study.

Treatment procedure. Steroid treatment (dexasone) was started during the first hour after laser exposure and was repeated daily following radiation. Daily does was 0.5 mg/kg weight i.m.

Results

(1) Prostanoid involvement following sham exposure.

The effect of sham exposure on PGE_2 levels in the vitreous and retina-choroid is depicted in Table 1. A transitory significant increase in PGE_2 production by the retina-choroid of the eyes exposed to illumination for a short period of time equal to one laser lesion, occurred 1 hour after exposure. However, in eyes subjected to illumination for a long period of time, equal to 30 laser burns, a significant increase in PGE_2 production by the retina-choroid occurred only 7 days after exposure. In both groups retinal PGE_2 production was within control limits at all other time points measured.

It is necessary that these results be reproduced in a larger number of samples before any conclusion can be drawn, as sample size was small and the standard deviation exceeded 50% of the mean.

In eyes subjected to a short sham exposure, an increase in vitreal PGE_2 levels was noted only at the 1 hour interval, whereas in eyes sham exposed for a longer time, vitreal PGE_2 levels remained unchanged from controls at all time intervals. Again, in order to clarify this observation, more samples are required.

Protein levels in the vitreous of eyes subjected to sham exposure are depicted in Table 2. Following long sham exposure, a significant increase in vitreal protein levels occurred at the 3 day interval, although levels remained within control limits at the remaining time intervals studied. On the other hand, with a short exposure period, significant increase in vitreal protein levels was noted already at the 1 hour interval, and levels remained elevated above controls at the 24 hour time interval. Later, at 3 days and at 14 days, vitreal protein levels returned to within control limits.

(2) Steroid treatment of a single suprathreshold argon laser-induced retinal burn.

The effect of steroid treatment of PGE_2 production by the retina-choroid and on PGE_2 vitreal levels following a single suprathreshold laser lesion is given

in Table 3. In the eyes that were not treated with steroids, a significant biphasic increase in retinal-choroid PGE_2 production was noted. The first peak occurred 1 hour following the laser burn, with levels remaining elevated at the 1 day time interval. A second peak in PGE_2 production by the retina-choroid was noted at the 14 day interval. In the steroid-treated rabbits, this biphasic increase in production did not occur, and PGE_2 levels remained within control limits at all time intervals examined.

Protein levels in the vitreous following a single laser burn in untreated and laser exposed steroid-treated rabbits are shown in Table 4. Vitreal protein levels in rabbits not given steroids and exposed to a single retinal burn showed a biphasic increase evident at 1 hour and at 14 days after laser application; they remained unchanged compared to control levels at the other follow-up periods. In steroid-treated rabbits, no such biphasic increase in vitreal protein levels occurred, and levels remained unchanged when compared to controls throughout the follow-up period.

(3) Preliminary results for multiple subthreshold argon laser-induced retinal burns and prostanoid involvement.

PGE_2 production by the retina-choroid following multiple subthreshold laser retinal burns as well as PGE_2 and protein vitreal levels are depicted in Table 5. PGE_2 production by the retina-choroid in this group was significantly elevated at 1 hour following exposure and remained at this higher level at the 1 day follow-up point. It returned to control level at 2 days, but at the 3 day and 7 day time intervals, retina-choroid PGE_2 production was again significantly augmented compared to control levels.

PGE_2 vitreal levels of eyes exposed to multiple subthreshold laser retinal applications were sugnificantly augmented at the time intervals coincideing with the peaks in PGE_2 production by the retina-choroid. It is noteworthy that at time intervals later that 1 hour, for both retinal and vitreal PGE_2 levels, the sample number was smaller than usual and did not exceed 11; thus, further studies are required to achieve conclusive data.

Vitreal protein levels following multiple subthreshold laser exposure were not elevated above control levels at all time intervals. An earlier evaluation using 11 samples of vitreal protein levels at the 1 hour interval showed a significant increase; however, when a larger number of samples (19) was evaluated, protein levels did not exceed control limits. Further study to clarify this difference is required.

Discussion

The present work investigated the effect of argon laser application to the retina and sham exposure on PGE_2 production by the retina-choroid as well as vitreal PGE_2 and protein levels at various time intervals after exposure. In addition, the effect of steroid treatment in eyes subjected to retinal laser application was studied.

Two different retinal injuries were produced:

(1) a single laser burn using suprathreshold energy levels;

(2) multiple (30) laser burns using subthreshold energy levels.

Two different sham exposure durations were used:

(1) short sham exposure -- a period coinciding with the time required for a single retinal laser exposure;

(2) long sham exposure -- a period coinciding with the time required for 30 retinal laser applications.

This discussion will be dealing mostly with results obtained by us during 1984 and the present year, since there is no data regarding changes in arachidonic acid metabolism following laser application to the retina in the scientific literature.

Production of a single retinal laser burn using above-threshold energy levels caused a biphasic increase (day 1 and 14) in PGE_2 production by the damaged retina-choroid, with a significant accumulation of protein in the vitreous at the time intervals corresponding to the peaks in retinal PGE_2 production. However, the first peak in vitreal protein levels, evident at 1 hour after exposure, was shorter than the retinal PGE_2 peak, and control levels were resumed at 1 day. It is noteworthy that vitreal PGE_2 levels of eyes exposed to a single laser burn remained unchanged from control levels.

Results of the present study using a single suprathreshold energy burn may be compared with those of the previous work performed during 1984 using similar suprathreshold energy levels for each of the 30 retinal lesions applied widely set apart (Table 6).

Multiple suprathreshold argon laser applications were associated with a similar biphasic augmentation of retinal PGE_2 production, evident at different time intervals (days 1 and 3). PGE_2 amounts at the second peak were three to four fold higher than either peak following a single laser burn.

The biphasic increase in PGE_2 retinal production following multiple laser exposure was associated with a similar increase in vitreal PGE_2 levels, while following a single laser application, vitreal PGE_2 amounts were not elevated when compared to controls.

Protein vitreal levels following multiple above threshold retinal laser exposures were increased above control levels at 1 hour and remained elevated during the follow-up period up to 14 days. After a single laser application an elevation in vitreal protein levels occurred only twice, coinciding with the two peaks of increased retinal PGE_2 production (1 hour and 14 days). PGE_2 levels in the retina-choroid following multiple subthreshold exposure were elevated at all time intervals up to day 7, except for day 2. This increase extended over longer periods of time compared to that following the other laser-induced retinal injuries. Following subthreshold exposure the increase in vitreal PGE_2 levels obtained coincided with the increase in retinal PGE_2 production, and levels were 1.5 to 2.5 times higher than PGE_2 levels observed after multiple suprathreshold exposure.

It is noteworthy that subthreshold exposure was not followed by an increase in vitreal protein levels at all time intervals, while suprathreshold exposure resulted in an increase in protein levels evident at all time intervals up to 14 days.

Sham Exposure. Sham exposure for short and long periods resulted in a significant elevation in PGE_2 production by the retina-choroid, at 1 hour and at 7 days, respectively. PGE_2 accumulation in the vitreous coincided with retinal PGE_2 elevation and was above control levels at 1 hour only following short exposure. An increase in vitreal protein levels occurred earlier (1 hour, 1 day) following short exposure (1 hour) and later (3 days) following longer exposure. More data on PGE_2 involvement following sham exposure are required before definite conclusions can be drawn.

Effect of steroid treatment on a single retinal laser burn. Steroid treatment of rabbits exposed to a single suprathreshold laser application inhibited the biphasic increase in PGE_2 production by the retina-choroid, otherwise observed in untreated eyes exposed to similar energy levels. Likewise, in steroid-treated rabbits exposed to a single laser burn, PGE_2 accumulation in the vitreous, observed twice (1 hour and 14 days) in untreated exposed eyes, was inhibited altogether. Thus, in steroid-treated eyes exposed to a single lase burn, PGE_2 production by the retina-choroid as well as vitreal PGE_2 and protein levels were unchanged from control levels.

Summary of Discussion

In summary, the present investigation examined the effect of argon laser application on the retina-choroid and vitreous. Various energy levels were used: Single suprathreshold burn, multiple (30) suprathreshold burns, and multiple (30) subthreshold burns. In each case, three parameters were measured

at 1 hour, 1 day, 2 days, 3 days, 7 days and 14 days after exposure: (1) PGE_2 production by the retina-choroid; (2) PGE_2 levels in the vitreous; and (3) protein levels in the vitreous. Changes following sham exposure of short duration (equal to one laser burn) or long duration (equal to multiple laser burns) and the effect of steroid treatment on the laser-induced retinal damage were studied as well.

(1) PGE_2 production by the retina-choroid. Eyes exposed to supra-threshold energy levels (single or multiple burns) showed a biphasic increase in PGE_2 production by the retina-choroid. The peaks occurred on days 1 and 14 following a single exposure and on day 1 and 3 after multiple applications. In eyes subjected to sub-threshold energy levels, the increase in PGE_2 production by the retina-choroid was of longer duration, extending from the first hour after exposure through day 7, with the exception of day 2. In eyes subjected to sham exposure, PGE_2 production by the retina-choroid peaked only once: immediately after short exposure and on day 7 after long exposure.

(2) PGE_2 levels in the vitreous. Following a single supra-threshold laser application and following sham exposure of long duration, vitreal PGE_2 levels remained unchanged from controls, despite the biphasic increase in retinal PGE_2 production in these eyes. However, multiple applications, at both supra- and sub-threshold energy levels, were followed by an increase in vitreal PGE_2 coinciding with the increase in retinal PGE_2 production at these levels. Corresponding increases in vitreal PGE_2 levels and retina-choroid PGE_2 production were also noted after sham exposure of short duration.

(3) Protein levels in the vitreous. Eyes subjected to a single suprathreshold laser application showed an augmentation in vitreal protein levels coinciding with the increase in retinal PGE_2 production. Multiple suprathreshold exposure elicited an increase in vitreal PGE_2 levels that was of longer duration than the corresponding biphasic increase in retinal PGE_2 production. However, after multiple subthreshold exposures, there was no enhancement in vitreal protein levels, despite the prolonged increase in retina-choroid PGE_2 production in these eyes. Eyes subjected to sham exposure for short duration also showed an increase in vitreal protein levels coinciding with the increase in PGE_2 production by the retina-choroid.

(4) Effect of steroid treatment on laser-induced retinal damage. In eyes treated with steroids following exposure to a single suprathreshold laser application, retinal PGE_2 levels, as well as vitreal PGE_2 and protein levels, remained unchanged compared with controls.

Clinical significance; Laser induced retinal injury as demonstrated by us is associated with an inflammatory reaction, manifested by accumulation of PGE_2 and protein in the vitreous, as PGE_2 produced in excess by the damaged retina/choroid are accumulating in the vitreous. Steroid treatment effectively inhibited the inflammatory reaction of laser induced retinal damage, as in the steroid treated group normal vitreal PGE_2 and protein levels were maintained throughout a two week follow up period. The inhibitory effect of steroid treatment on the inflammatory reaction was related to reduction in PGE_2 production by retina/choroid. The clinical significance of our study lies in the demonstration of the efficacy of steroid treatment in inhibiting the laser induced inflammation when started immediately after exposure. However other medication should be sought for complete inhibition of prostaglandin production at the later stages after exposure.

A better inhibition of prostoglandin production might be achieved by using various other nonsteroidal antiflammatory drugs, alone or in combination with steroids A's.

In conclusion

The above findings relate not only to the prostaglandin metabolism relationship to laser retinal injuries, but also to other cardinal isues in the physiology and traumatology of the eye such as the determination of the actual threshold of retinal laser injuries the pathogenesis, therapy and healing of these lesions and the normal functions of the blood retinal barrier and the results of its disruption.

Points for further investigation

(1) What is the reason for the biphasic increase in retinal PGE_2 production following suprathresold laser exposure?

(2) What is the underlying cause for the prolonged increase in retinal PGE_2 production following subthreshold exposure?

(3) In eyes subjected to subthreshold energy levels, what is the mechanism that allows for the differential accumulation of PGE_2 and protein in the vitreous?

(4) Does the microscopic appearance of eyes subjected to laser exposure bear a relationship to the change in PGE_2 metabolism by the retina-choroid?

(5) Does steroid treatment also affect PGE_2 metabolism following subthreshold exposure?

Table 1. Prostaglandin E_2 levels in retina-choroid and vitreous at different time intervals following sham exposure.

	Prostaglandin E_2 Levels (pg/mg weight) (mean±SD)					
	Retina-Choroid			Vitreous		
Time after exposure (days)	Control	Long Exposure	Short Exposure	Control	Long Exposure	Short Exposure
0*	360±137 n=37**			7476±4770 n=30		
1/24 (1 hr)		437±228 n=30 NS***	1291±921 n=18 p<0.03****		3361±2009 n=32 NS	16476±7569 n=20 p<0.03
1		455±223 n=26 NS*	507±261 n=27 NS		5848±2290 n=41 NS	7381±3238 n=21 NS
3		353±134 n=30 NS	363±129 n=14 NS		3355±1328 n=30 NS	7243±2968 n=10 NS
5		377±152 n=16 NS			3403±1522 n=16 NS	
7		1047±480 n=12 p<0.03			9384±6013 n=12 NS	
14		433±146 n=30 NS	534±245 n=28 NS		4549±2429 n=32 NS	4666±2374 n=31 NS

* Control levels (untreated animals).
** n indicates number of eyes involved.
*** NS = not statistically significant.
**** p = value for Student's t-test comparing levels in each group with corresponding control levels.

Table 2. Protein levels in vitreous of eyes subjected to sham exposure

Protein Levels (pg/mg weight) (mean+ SD)

Time after exposure (days)	Control	Long Exposure	Short Exposure
0*	164±0.4 n=30**		
1/24 (1 hr)		1.91±0.7 n=30 NS***	1.99±0.37 n=20 p<0.003****
1		1.7±0.41 n=40 NS	2.06±0.34 n=27 p<0.03
3		1.9±0.4 n=30 p<0.03	1.7±0.44 n=18 NS
5		1.8±0.5 n=18 NS	
7		1.3±0.38 n=12 NS	
14			1.8±0.64 n=31 NS

* Control levels (untreated rabbits).
** n indicates number of eyes involved.
*** NS = not statistically significant.
**** p = value for Student's t-test comparing levels in each group with corresponding control levels.

Table 3. Effect of steroid treatment of retina-choroid prostaglandin E_2 production and vitreal prostaglandin E2 levels following signle suprathreshold laser lesion.

	Prostaglandin E_2 Levels (pg/mg weight) (mean+SD)			
	Retina-Choroid		Vitreous	
Time after Exposure (days)	Untreated	Steroid Treated	Untreated	Steroid Treated
0*	360±137 n=37**		7476±4770 n=30	
1/24 (1 hr)	729±210 n=23 p<0.03***		3366±595 n=24 NS****	
1	788±232 n=19 p<0.03	262±127 n=12 NS	4654±2141 n=20 NS	4401±1594 n=12 NS
3	453±235 n=22 NS	397±164 n=20 NS	3792±2137 n=20 NS	5753±2723 n=22 NS
7	.			7668±2844 n=11 NS
14	637±267 n=19 NS		4660±2447 n=23 NS	5083±1900 n=12 NS

* Control levels (untreated animals).
** n indicates number of eyes involved.
*** NS = not statistically significant.
**** p = value for Student's t-test comparing levels in each group with corresponding control levels.

Table 4. Effect of steroid treatment on vitreal protein levels following single laser application.

Time after Exposure (days)	Protein Levels (pg/mg weight) (mean±SD) Untreated	Steroid-Treated
0*	164±0.4 n=30**	
1/24 (1 hr)	2.03±0.6 n=24 p<0.003***	
1	1.74±0.49 n=20 NS****	2.06±0.34 n=18 NS
3	1.9±0.52 n=22 NS	1.7±0.38 n=22 NS
14	2.0±0.5 n=23 p<0.03	1.5±0.4 n=12 NS

* Control levels (untreated animals).
** n indicates number of eyes involved.
*** NS = not statistically significant.
**** p = value for Student's t-test comparing levels in each group with corresponding control levels.

Table 5. Subthreshold laser retinal damage - effect on prostaglandin E_2 and protein levels in vitreous and retina-choroid at different time intervals.

Time after Exposure (days)	Prostaglandin E_2 Levels (pg/mg weight) (mean+SD) Retina-Choroid	Prostaglandin E_2 Levels (pg/mg weight) (mean+SD) Vitreous	Protein Levels (pg/mg weight) mean+SD) Vitreous
0*	360±137 n=30**	7476±4770 n=30	1.64±0.6 n=30
1/24 (1 hr)	785±373 n=18 p<0.03***	15339±5895 n=19 p<0.03	
1	1443±641 n=9 p<0.03	23705±4206 n=9 p<0.03	1.6±0.35 n=19
2	296±185 n=11 NS****	9153±5458 n=11 NS	1.7±0.4 n=10
3	1001±423 n=11 p<0.03	12301±8185 n=11 p<0.03	1.7±0.49 n=11
7	1010±593 n=6 p<0.03	15583±6929 n=6 p<0.03	1.7±0.16 n=6

* Control levels (untreated animals).
** n indicates number of eyes involved.
*** NS = not statistically significant.
**** p = value for Student's t-test comparing levels in each group with corresponding control levels.

Table 6. Prostaglandin E_2 production by the retina-choroid and vitreal prostaglandin E_2 and protein levels at different time intervals following multiple above threshold laser applications.

	Retina-Choroid	Vitreous	
Time After Exposure (days)	Prostaglandin E_2 (pg/mg weight) (mean±SD)	Prostaglandin E_2 (pg/mg weight) (mean±SD)	Protein (pg/mg weight) (mean±SD)
0*	360±137 n=30**	7476±4760 n=30	1.64±0.4 n=30 p<0.03**
1/24 (1 hr)	1031±360 n=21 p<0.03	9900±3841 n=32 p<0.03	2.04±0.45 n=32
1	518±212 n=34	9132±1731 n=34	2.6±0.6 n=34
2	432±279 n=19	4986±2624 n=32	2.2±0.79 n=19
3	3098±1423 n=35 p<0.03	±8184 n=44 p<0.03	2.09±0.56 n=46
5	449±218 n=16	5910±3557 n=16	2.0±0.23 n=16
7	550±199 n=24	3882±2119 n=24	2.0±0.4 n=23

* Value of control levels - untreated animals.
** n indicates number of eyes involved.
**** p = value for Student's t-test comparing levels in each group with corresponding control levels.

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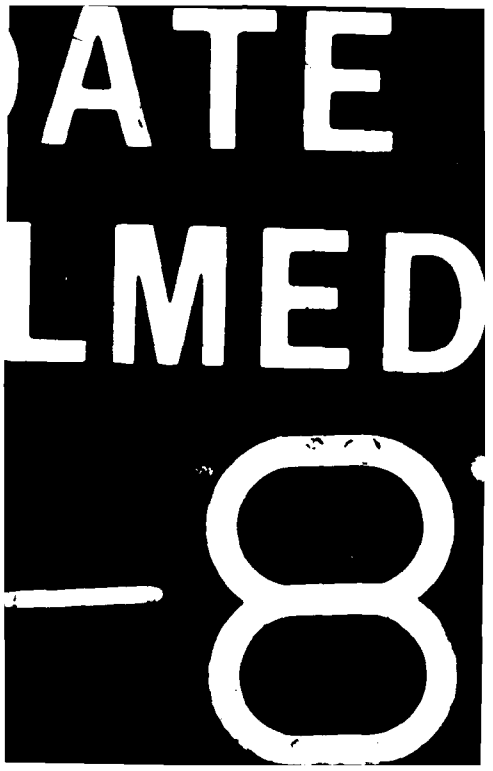
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